

Biomarkers for therapy with the EGFR inhibitors

Helmout Modjtahedi

Kingston University London, UK

Since the early 1980s, abnormal expression and activation of the epidermal growth factor receptor (EGFR) family members, in particular EGFR and HER-2, have been reported in a wide range of human epithelial malignancies and in some studies have been associated with poor clinical outcomes. These discoveries have led to the strategic development of several types of inhibitors. Some of these inhibitors namely anti-EGFR monoclonal antibodies [(mAbs) cetuximab and panitumumab], anti-HER-2 mAb trastuzumab, small molecule EGFR tyrosine kinase inhibitors [(TKIs) gefitinib, erlotinib], or a dual EGFR and HER-2 TKI (lapatinib), have been approved by the FDA for the treatment of patients with head and neck, metastatic colorectal, pancreatic, breast cancers or gastric cancers. Despite these advances, two major outstanding challenges associated with the use of the EGFR inhibitors are the lack of reliable predictive markers for response to therapy with the EGFR inhibitors and the duration of response which can be short in some of these patients. In some studies, the presence of EGFR gene amplifications or somatic mutations, mutated KRAS or PTEN, the expression of autocrine EGFR ligands (e.g. epiregulin, amphiregulin), other members of the EGFR family (e.g. HER-2, HER-3) or heterologous growth factor receptor (e.g. IGF-IR and c-Met) or development of skin rash were associated with the response or resistance to treatment with the EGFR inhibitors. However, all patients with wild type KRAS, for example, do not respond to therapy with the EGFR inhibitors. In this presentation, I shall discuss these challenges and developments to date regarding the establishment of more reliable predictive markers for response to therapy with the EGFR inhibitors.

Biography

Dr Helmout Modjtahedi is Reader in Cancer Therapeutics at Kingston University London. He completed his PhD (1989-1993) followed by 6 years of postdoctoral studies at The Institute of Cancer Research, University of London. In 1999, he joined University of Surrey as a Clinical Lecturer in Tumor Immunology and in 2007 moved to Kingston University London. His research to date has been focused upon targeting of EGFR family members with monoclonal antibodies and small molecules tyrosine kinase inhibitors. He has published more than 50 papers and book chapters and is serving as an editorial member on several journals.